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10/723,091	11/25/2003	Jose Remacle	4044.001	7897

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,091	REMACLE ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5 and 7-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-5 and 7-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1, 4-5 and 7-21 are pending and under examination.

Withdrawn Rejections

In view of the amendments to the claims and applicants' arguments, the 35 USC 112, first and second paragraphs and 35 USC 102 over Stillman rejections have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-5 and 7-21, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification states at [0039]:

> The polyols may be cyclic or may have a linear backbone and may contain atoms/groups other than hydroxy and hydrogen, and may be either the D or L enantiomer. The polyols may

> also be linked to other molecules by an alcohol function or by another function. For example, sorbitol is linked by its C4 alcohol to alpha-D glucose to form maltitol.

Accordingly, it is unclear as to the claimed "other molecules" that is linked to maltitol or mannitol since the specification describes maltitol as the resultant linkage between sorbitol and glucose. The single molecule, sorbitol linked to the single molecule "alpha-D glucose" would not provide a written description for the huge scope of "other molecules" linked to maltitol, mannitol and sorbitol. Thus, the specification does not describe the other kind or type of other molecules encompassed by the huge scope of the claimed "other molecules" other than the single disclosed glucose. There is no description that correlates this single disclosed molecule to other molecule or to any other molecules. More importantly, it does not describe a method by which this is contacted to an array such that the contact results in a stable array.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-5 and 7-21, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 1, step a) is not clear whether mannitol, maltitol or sorbitol is the linked polyol or unlinked polyol that is being linked to other molecules to produce mannitol, maltitol or sorbitol. Clarification/explanation is required.

2. Claim 1 is indefinite as to the metes and bounds of the claimed "other molecules". The specification does not define what is included or precluded by said other molecules, absent distinguishing or characterizing features of said "other molecules".

Claim Rejections - 35 USC § 103

Claims 1, 4-5 and 7-21, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Decker(GB 2,016,687A) or Devereaus (WO 93/07466) or Stillman (20030175827) in view of either Guo(Faming Zhuanli Shenqing Gongkai) or Sandford (US 2003/0134294) and Schultz et al(20040198637) for reasons of record as reiterated below.

Stillman discloses at paragraph [0010] a method for producing a thin film dried protein composition comprising

making a protein containing solution that is to be dried on a surface, preferably a biologically active protein. The term "biologically active" includes any protein that can participate in a specific binding reaction, (such as antibodies, antibody fragments, antigens, antigen fragments), as well as peptides or enzymes.) The solution is made with a buffer that maintains the surface pH between about 5.0 and 9.0 during solution drying and with a saccharide in an amount sufficient to stabilize the protein during solution drying. The solution is then applied to a support having the surface for depositing. Thin film of protein containing solution is allowed to dry on the support surface under normal pressures. At paragraph [0011] the method enables one to make stable thin film dried protein compositions. Such films can be incorporated into protein analytical devices. of particular interest are proteomic microarrays.

Stillman discloses at [0026] referring to FIG. 3;

> A series of compositions were tested including a PBS/5% trehalose/10% methanol solution containing 1.5 mg/ml of antibody protein. The difference amongst the solutions was the saccharide used, namely, glucose, ***mannitol***, xylose, trehalose, maltodextrin, and glucuronic acid. Spotted and dried solution spots were tested for shelf life, i.e., the retention of biological activity, in this case, a specific binding reaction. While some saccharides delivered a higher specific signal than others, all delivered a signal at least twice that of the control solution which did not contain any saccharide.

Decker discloses at pages 2 up to 5 an immunoassay method for the detection and determination of antigens and antibodies. The method comprises an indirect application of an antibody or antigen to a solid support (a selected capture protein, as claimed). It generally involves the procedure in which the solid support is precoated with antigen or antibody to potentiate the adherence of the antibody or antigen. The reagents consist of a solid support that has been coated either directly or indirectly with an antigen or antibody and stabilized with a sugar coating to impart a storage capability. The percent of sugar e.g., xylitol, mannitol and sorbitol is given in Table II.

Devereaus discloses at e.g., page 14, line 16 up to page 15, line 25 a method (i.e., the use of .1-50% of polyol, specifically arabitol and xylitol). See specifically the EXAMPLES, which provide a detail description of the claimed method using specific components in the array.

Each of Decker, Stillman and Devereaus do not disclose the use of antiseptic as sodium azide and that the protein is covalently linked to the solid support. However, Guo discloses in the abstract a method in which a protein chip with array of 10-10,000 cm-1 and array size of 5-500 consists of the activated carrier and spotting solution. The spotting solution is composed of probe (such as antigen, antibody, drug receptor,

agglutinin, cell, or tissue), fucose, antiseptic (such as Na azide) and C2-10 aliphatic polyol. The protein chip is manufactured by spotting the mixture of probe and spotting solution on the activated carrier sheet, and then blocking with bovine serum. The protein chip may be used to detect, recognize, and identify the antigen, antibody, medicine or its receptors, polysaccharide, agglutinin, tissue, or cell.

Sandford discloses at paragraph [0197] that preservatives like azide are effective to retard or prevent microbial proliferation. Sandford discloses at paragraph [0199] that lyoprotectants are effective to reduce or prevent chemical or physical instability of a protein upon lyophilization and storage. Examples of a polyol such as trihydric or higher sugar alcohol (e.g., glycerin, erythritol, glycerol, arabitol, xylitol, sorbitol, and mannitol). Sandford also discloses the use of borate buffer.

Schultz et al discloses:

> [0101] In one embodiment, the polypeptides are provided in a reaction mixture that is suitable for the necessary reaction between the reactive group on the unnatural amino acid side chain and the reactive group attached to the solid support. ….. In some embodiments, the polypeptides remain hydrated throughout the preparation, storage, and assaying of the array to prevent denaturation of the polypeptide. Accordingly, humectants or polymers such as glycerol, polyethylene glycol, glycerin, **maltitol**, polydextrose, sorbitol, cetyl alcohol, fatty alcohols, propylene glycol,

and the like, can be used to prevent evaporation of the nanodrops.

[0048] Systems for immobilizing polypeptides on a solid support, as well as the resulting solid supports containing the polypeptides, e.g., protein arrays, are provided. The systems allow one to covalently or non-covalently attach the polypeptides to the solid support in such a manner as to preserve the function of the polypeptides or to regain their functionality once attached. The ***covalent or non-covalent attachment generally does not substantially affect the structure, function, or activity of the polypeptide (e.g., catalytic activity, ability to bind other polypeptides, ability to bind nucleic acids, ability to bind small molecules, 3-D structure, etc.)***. The protein arrays of the invention are versatile and can be adapted to a variety of protein analysis formats. The arrays find use in a wide variety of applications, including numerous types of screening protocols and any protein analysis where high throughput parallel analysis is desirable.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use azide in the method of either Decker or Stillman or Devereaus as taught by either Sandford or Guo. The advantages taught by Sandford or Guo would provide the motivation to one having ordinary skill in the art as to the known use of azide as a preservative. Furthermore, as taught by Schultz the protein can be covalently or non-covalently link to the array in a manner that preserves its function.

Response to Arguments

Applicants recognize that Stillman et al., (D3; US 200310175827) discloses a method for the preparation of a stable

thin film dried protein composition on an inert surface of e.g. a solid support (surface having a protein denaturing capability, cf. claim 1). A thin film of a protein containing solution is applied to the surface of a solid support together with a saccharide, such as xylitol or mannitol, for stabilizing the protein during drying. But argue that Stillman et al. fails to teach covalent binding of the capture proteins on the support, as is recited in the currently amended claim 1.

Applicants state that even if Schultz teaches covalent or non-covalent linking however Schultz was filed after the filing date of the present application; the present application was filed on November 25, 2003, and then Schultz was filed on December 22, 2003. Hence, Schultz is an improper reference under 35 U.S.C. §103. Without Schultz, the combination of references fails to teach or suggest all of the elements of the claimed embodiments.

In response, Schultz claims priority to the earlier filed provisional application filed on Dec. 22, 2002, which predates the instant application filing date of 11/25/2003. Hence, Schultz is a properly used prior art. See MPEP 706.02 (V)(D) which states:

> (D) If the application properly claims benefit under 35 U.S.C. 119(e) to a provisional application, the effective filing date is the filing date of the provisional

application for any claims which are fully supported under the first paragraph of 35 U.S.C. 112 by the provisional application.

Accordingly, the combined teachings of the references e.g., Stillman and Schultz would lead one having ordinary skill in the art to the claimed covalent linking of the capture proteins to the support.

Applicants argue that Guo has been improperly relied on the English language abstract. Applicants cite MPEP at section 706.02 Part II:

When an abstract is used to support a rejection, the evidence relied upon is the facts contained in the abstract, not additional facts that may be contained in the underlying full text document. Citation of and reliance upon an abstract without citation of and reliance upon the underlying scientific document is generally inappropriate where both the abstract and the underlying document are prior art. See Exparte Jones, 62 USPQ2d 1206, 1208 (Bd. Pat. App. & Inter. 2001) (unpublished). To determine whether both the abstract and the underlying document are prior art, a copy of the underlying document must be obtained and analyzed. If the document is in a language other than English and the examiner seeks to rely on that document, a translation must be obtained so that the record is clear as to the precise facts the examiner is relying upon in support of the rejection. [Emphasis added.]

In reply, MPEP states, the abstract, can be relied as evidence if the facts are contained therein. The abstract clearly recites the azide as a preservative, as is well known in the art as evident from Sanford teachings above. Thus, since the abstract sufficiently discloses azide hence, its reliance

instead of the full text document suffices. (Note even without Guo, Sanford above also discloses the used of azide, which is used for the same purpose as applicants use azide i.e., as a preservative).

Applicants argue that the remaining references, Decker et al. (D1, GB 2016687) neither mentions a protein deposition on discrete regions of the solid support nor that the proteins are covalently attached to the support. Additionally, Decker et al. fails to teach the order of method steps, i.e. Decker et al. mentions a stabilization step subsequent a coating step with protein (cf. Decker at al. p.2, 1. 12 to 15). In contrast, new claim 21 discloses contacting of the polyol and protein with the solid support in the same step.

Like Decker et al., Devereaux et al., (D2, WO 93/07466) does not mention a protein deposition on discrete regions of the solid support. Further, Devereaux does not disclose contacting of polyols and capture probes with the solid support. Sandford (D5, US 2003/0134294 or WO 03/050234) is introduced by the Examiner to provide motivation to use a borate buffer in the solution of e.g. Stillman. Sandford does not disclose, as is recited in new claim 21, contacting a protein and a linear polyol selected from the group consisting of mannitol, maltitol

and sorbitol, with the support in a single step. Sanford further does not specify drying of the spotting solution. Additionally, Sandford does not mention a protein deposition on discrete regions of the support. Moreadith (D6, US 6,632,934) neither mentions protein arrays nor specifies the usage of linear polyols selected from the group consisting of mannitol, maltitol and sorbitol for stabilizing arrays.

In response, one cannot show non-obviousness by attacking the references individually where the rejection is based on a combination of references. In re Young, 159 USPQ 725 (CCPA 1968). The test for obviousness under 35 USC 103 is not the express suggestion of the claimed invention in any or all of the references but what the references taken collectively would suggest; and inferences which one skilled it in the art would reasonably be expected to drawn from the disclosure in the references. In re Preda, 159 USPQ 342 and In re Conrad, 169 UASPQ 170. The claims ("being present on an array, claim 1) also recite in the alternative applying the protein directly on the support, after which the polyol is spotted on the surface. It is unclear as to how the method steps of Decker are in different order. As clearly discussed above by applicants the protein of Decker is applied directly to a solid support and then sugar is added on the surface.

Since applicants present the same arguments to rebut Devereaus, hence the response under Decker above is applied to Devereaus.

Sanford is employed not for the purpose as argued since the primary references e.g., Stillman discloses the method of mixing of the spotting solution for the microarray. Rather, Sanford is used for its disclosure of using a borate buffer and the

motivation for one having ordinary skill in the art to include a borate in the solution of e.g., Stillman.

Likewise, Moreadith is employed not for the purpose as argued, since e.g., Stillman discloses said protein deposition on arrays. Rather Moreadith is used for its disclosure at col. 24, lines 23-35. That is, in general, due to the relative stability of peptides, they may be readily stored in aqueous solutions for fairly long periods of time if desired, e.g., up to six months or more, in virtually any aqueous solution without appreciable degradation or loss of antigenic activity. However, where extended aqueous storage is contemplated it will generally be desirable to include agents including buffers such as Tris or phosphate buffers to maintain a pH of about 7.0 to about 7.5. Moreover, it may be desirable to include agents which will inhibit microbial growth, such as sodium azide. For extended storage in an aqueous state it will be desirable to store the solutions at about 4.degree. C., or more preferably, frozen. Of course, where the peptides are stored in a lyophilized or powdered state, they may be stored virtually indefinitely, e.g., in metered aliquots that may be rehydrated with a predetermined amount of water (preferably distilled) or buffer prior to use. Accordingly, the combined teachings of the prior art renders the claimed prima facie obvious at the time the invention was made.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf

Primary Examiner
Art Unit 1639

tdw
July 27, 2007